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High Specific Activity [^{11}C]Phosgene from [^{11}C]Carbon Monoxide

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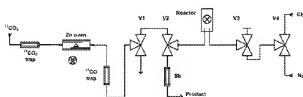
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Introduction. [^{11}C]Phosgene is a versatile reagent for labelling PET radiopharmaceuticals. A few sites has established the production of [^{11}C]phosgene routinely and attempts to improve its preparation persevere.

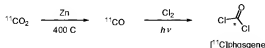
We have been investigating scaled-down photochemical preparation of [^{11}C]phosgene, focusing on increasing specific radioactivity (SA) and the stability of production. For increasing SA we sought to minimize isotopic dilution through reducing reaction volumes and associated amounts of reagents.

Methods. To accomplish the synthesis several valves were added to our [^{11}C]carbon monoxide system. Accurate, batch-wise delivery of [^{11}C]carbon monoxide enabled minimizing the size of the photo-reactor; so the amount of chlorine was accordingly reduced.



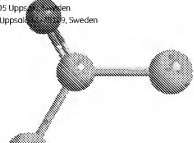
Simplified schematic drawing of the synthesis module

First, [^{11}C]carbon dioxide is reduced over zinc to [^{11}C]carbon monoxide, which is further directed to a photo-reactor charged with chlorine gas. Photochemical generation of [^{11}C]phosgene is initiated by a UV lamp. After a 1-5 min the reaction gas mixture is swept to a vial charged with a solution of aniline to trap [^{11}C]phosgene. Excessive chlorine is removed with an antimony tower. The activity that is not retained in the aniline solution is further trapped on an appropriate solid-phase column.



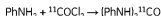
Key steps in the photoinitiated formation of phosgene from carbon monoxide:

- 1) $\text{Cl}_2 + h\nu \rightarrow 2\text{Cl}\cdot$
- 2) $\text{Cl}\cdot + \text{CO} \leftrightarrow \text{ClC(O)}\cdot$
- 3) $\text{ClC(O)}\cdot + \text{M} \rightarrow \text{CO} + \text{Cl}\cdot + \text{M}$
- 4) $\text{ClC(O)}\cdot + \text{Cl}_2 \rightarrow \text{COCl}_2 + \text{Cl}\cdot$
- 5) $\text{COCl}_2 + \text{Cl}\cdot \rightarrow \text{ClC(O)}\cdot + \text{Cl}_2$
- 6) $\text{ClC(O)}\cdot + \text{Cl}\cdot \rightarrow \text{CO} + \text{Cl}_2$
- 7) $2\text{Cl}\cdot \rightarrow \text{Cl}_2$



Results. The decay-corrected radiochemical yield of [^{11}C]phosgene reached 70–85% after three-minute irradiation of the reaction mixture at room temperature. Specific radioactivity was ≥ 200 GBq/ μmol , measured at the end of synthesis of [^{11}C]phosgene. Separate experiments confirmed that isotopic dilution during the labelling synthesis was negligible.

Discussion. Phosgene is a very reactive compound, which may explain the sensitivity of [^{11}C]phosgene-mediated labelling to external factors such as tracers of water, etc. To evaluate performance during optimization we used the following test reaction, which is known to be clean and instantaneous at room temperature, even in not strictly anhydrous conditions:



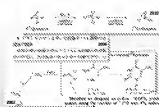
HPLC analysis of *N,N*-diphenylurea was also used for determining SA.

Described method proved to be convenient in terms of system setup and maintenance. Successive productions of [^{11}C]phosgene can be performed after several-minute conditioning of the system with He and N_2 .

Conclusion. [^{11}C]Phosgene was produced with high SA from [^{11}C]carbon monoxide using a small-sized remote-controlled unit. Since the process includes handling only gases it is operationally simple.

References

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